## REMARKS

Entry of the foregoing, reexamination and further and favorable reconsideration of the subject application in light of the following remarks, pursuant to and consistent with 37 C.F.R. § 1.112, are respectfully requested.

The Office Action Summary correctly indicates that claims 49-52, 57, 58, 60-63, 76, 77, 83, 84 and 108-123 are pending in the application and stand rejected.

Claims 49 and 120 have been amended to recite that the vector contains at least 20 consecutive amino acids of the recited sequence, which finds support at least in original claim 8. Claims 124-135 have been added to recite that the sequence which is at least 50% homologous with the sequence according to SEQ ID NO 1 in claims 57, 58, 61 and 120-122 is a sequence that is at least 70% to 80% or 95% homologous with the sequence according to SEQ ID NO 1, respectively. Claims 124-135 find support in at least original claim 3.

No prohibited new matter has been introduced by way of the above amendments. Applicants reserve the right to file a continuation or divisional application on subject matter canceled by way of this Amendment.

**Claim rejection under 35 USC § 112, written description**

Claims 49-52, 57, 58, 60-63, 76, 77, 83, 84 and 108-123 have been rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. The Office has acknowledged that a sequence according to SEQ ID NO 1 with an open reading frame from base pair 211 to base pair 1740 is adequately described. Office Action dated May 6, 2005 at 2. However, the Office has alleged that the claims embrace products containing sequences that do not meet the written description requirements and methods of using such products. The rejection is respectfully traversed.

***Concerning claims 49-52***

Claims 49-52 recite a biologically functional vector comprising a DNA sequence comprising at least 20 consecutive nucleotides of a selected sequence (49), or a vector comprising parts of different lengths comprising at least 20 bases of a selected sequence (50), or a ribozyme comprising two sequence sections of at least 10-15 base pairs that are complementary to a selected sequence (51).

The selected sequence of claims 49-52 is selected from the group consisting of a sequence according to SEQ ID NO: 1 with an open reading frame from base pair 211 to base pair 1740, and a sequence which hybridizes with the sequence according to SEQ ID NO: 1 under stringent conditions, wherein said DNA sequence is inversely oriented with respect to a promoter, and wherein said stringent conditions comprise hybridizing in a solution comprising 7% sodium dodecyl sulfate, 0.5M NaPO4, and 1 mM EDTA at pH 7.0 and 50°C and washing with a 1% sodium dodecyl sulfate solution at 42°C.

Thus, claims 49-52 are directed to nucleic acid molecules and vectors encoding antisense and ribozyme molecules. The function of the encoded molecules is related to the ability of sequences contained in the molecules to bind to segment(s) of sequences encoding fucosyl transferase, the enzyme encoded by SEQ ID NO:1. The recitation that the selected sequences are a sequence according to SEQ ID NO: 1 with an open reading frame from base pair 211 to base pair 1740 or a sequence which hybridizes with the sequence according to SEQ ID NO: 1 under stringent conditions particularly encompasses the genus of sequences that fulfill this function of the claimed molecules.

The structure of each of these nucleic acids is related to and defined by their function. A person of ordinary skill in the art at the time the application was filed would have been able

to recognize the structure of the genus of molecules of nucleotide sequence that would bind under stringent conditions to another given sequence, because the principles of DNA hybridization were well understood and the person of ordinary skill would have had a substantial level of skill in DNA hybridization.

Applicants have pointed out that the Office's own training materials on the subject of Written Description recognize that the genus of DNA sequences that bind to a reference sequence is sufficiently circumscribed by the requirement of stringent hybridization so that the genus is adequately described by the complete description of the reference sequence. *See, e.g.*, *Revised Interim Written Description Guidelines Training Materials* at Example 9, (http://www.uspto.gov/web/offices/pac/writtendesc.pdf)

> ("Now turning to the genus analysis, a person of skill in the art would not expect substantial variation among species encompassed within the scope of the claims because the highly stringent hybridization conditions set forth in the claim yield structurally similar DNAs. Thus, a representative number of species is disclosed, since highly stringent hybridization conditions in combination with the coding function of DNA and the level of skill and knowledge in the art are adequate to determine that applicant was in possession of the claimed invention.");

*see also, Synopsis of the Application of the Written Description Guidelines* at Example 9 (http://www.uspto.gov/web/menu/written.pdf). The Office has responded that the example provided in the training materials recited stringent conditions that are not identical to the conditions recited in the present claims.

The stringency conditions recited in the claims describe two steps with different temperatures and the temperature of 50°C in the first step provides for sufficient specificity so that sequences within the scope of the claims will specifically bind to SEQ ID NO:1. Although the Office training materials example used 6xSSC and 65°C as stringency conditions, a generalization over stringent conditions cannot define adequate specificity for a

any given sequence. Therefore, the correct application of the Office's own analysis of that example cannot be reasonably limited to just the conditions that are exemplified in the training materials.

In the present case, which requires a degree of homology to the exemplified sequences coding for the inventive activity, the conditions recited in the claims are sufficient to create specificity and were actually used by Applicant to identify fucosyl trasferase enzymes. (See Exhibit A: "Lab protocol of 20.8.96", 1 sheet – the portion between the marked !s.)

Furthermore the influence of SSC and SDS on hybridization and melting temperature cannot be considered identical. (See Exhibit B: "Current Protocols in Molecular Biology-suppl.", 2 sheets.) Differences in temperature may be offset by other factors in the recited conditions. Applicants respectfully submit that the recited parameters allow a background-free, accurate hybridization of the relevant nucleic acid molecules in a technically clear and unambiguous way. The Office did not adduce any sound scientific reason for the allegation that the conditions recited in the claims do not qualify as a high stringency condition for the claimed sequences, only that the recited conditions are not identical to the example in the Office training materials.

Claims 49-52 recite nucleic acids in various forms that satisfy a functional requirement of specifically binding with SEQ ID NO:1. This functional requirement also serves to define the structure of the genus to a person of ordinary skill. One skilled in the art would recognize that it is not necessary that the sequence(s), or partial sequence(s), contained in these constructs actually encode a protein having fucosyl transferase activity. Rather, the sequence need only hybridize with the target sequence. Therefore, a person of skill in the art

would recognize that the recited hybridization conditions are directly related to the functional aspects of the structure of the claimed vectors and DNA molecules.

The Office has responded that a person of ordinary skill would have to know the function of the sequence to which the claimed nucleic acids bind. However, the recited genus is defined by its ability to hybridize to SEQ ID NO:1, the function of which is well described by the specification. Therefore, the Offices response is misapplied to claims 49-52.

The genus of claimed sequences would have been recognizable to a person of ordinary skill in the art from the description of SEQ ID NO:1 and the knowledge of the structural features required for specific binding of complementary nucleic acids which are defined by a well described set of hybridization conditions. As a result, a person of ordinary skill would have recognized from the written description of the specification that the inventors were in possession of the invention defined by claims 49-52 at the time the application was filed. And accordingly, the written description requirement is met for these claims.

***Concerning claims 60, 62, 63, 76, 77, 83 and 84***

Claims 60, 62, 63, 76, 77, 83 and 84 depend from claim 51 and no grounds of rejection separate from the allegations directed at claims 49-52 have been alleged. Therefore, for at least the reasons set forth above the subject matter of these claims is also adequately described.

***Concerning claims 57, 58, 61, 63 and 108-119***

Claims 57-58 and 61 are independent claims directed to methods of preparing recombinant hosts comprising a vector expressing an antisense molecule or of preparing a recombinant host comprising a homologous recombination.

The issue of whether the written description requirement is satisfied for these independent claims must be decided upon the question of whether the steps that comprise the methods are described. The reasons that that Office has maintained the rejection appear to question whether the results of those steps are adequately described. Applicants respectfully submit that the Office has applied the wrong test. Applicants respectfully submit that the steps of the claimed methods are fully described and enabled. Therefore, the claimed methods are adequately described and enabled.

Claim 57 recites a step of identifying a DNA sequence in a host that codes for a protein having fucosyl transferase activity, the sequence comprising a selected DNA sequence having further defined characteristics. A biologically functional vector comprising at least 20 bases of the identified DNA sequence inversely oriented with respect to a promoter is then inserted into the host. Similarly, claims 58 and 61 recite a step of identifying a sequence encoding a protein having fucosyl transferase activity and additional defined characteristics and then using the identified sequence or portion(s) thereof. The selected sequences are further defined by being selected from among (A) a sequence according to SEQ ID NO: 1 with an open reading frame from base pair 211 to base pair 1740, (B) a sequence which is at least 50% homologous with the sequence according to SEQ ID NO 1, and (C) a sequence which hybridizes with the sequence according to SEQ ID NO: 1 under stringent conditions, wherein said stringent conditions comprise hybridizing in a

solution comprising 7% sodium dodecyl sulfate, 0.5M NaPO4, and 1 mM EDTA at pH 7.0 and 50°C and washing with a 1% sodium dodecyl sulfate solution at 42°C.

In maintaining the rejection, the Office appears to have misapprehended the point of Applicants argument. The Office has alleged that one in the art might not know from looking at a sequence that is 57% homologous to SEQ ID NO:1 whether the sequence had the function of SEQ ID NO:1 without screening for its activity. The allegation is irrelevant, because the claim includes the step of identifying a sequence, and the specification describes and teaches one how to identify a sequence.

***The steps of the method are fully described, whether or not every possible intermediate produced during the practice of the method is structurally defined.*** The claimed method recites the step of identifying a sequence that codes for a protein having fucosyl transferase activity, which may in some cases require a certain amount of routine screening. Whether or not the sequence is known *a priori*, the sequence can be determined, for example, as described in the specification and/or by any other method a skilled practitioner may employ with reference to the teachings of the specification. Following the identification step, a sequence derived from the identified sequence can be used to perform the remainder of the method as described.

The Specification describes how to identify the sequences and exemplifies the identification step, and in the process identifies a representative sequence. The identification step is fully described and can be performed on any of the recited hosts. At pages 18-19, the specification describes how to identify fucosyl transferase coding sequences in hosts using sequences from SEQ ID NO:1.

The Office has alleged that the specification does not provide sufficient guidance with respect to a conserved core structural motif. However, at page 6, the specification teaches

that the conserved sequence of SEQ ID NO:3 is particularly useful for sequence recognition. (See also, Exhibit C "Leiter et al. (1999)".) Leiter et al. functionally illustrates the cDNA sequence of the core fucosyltransferase.

Of course, the identification of a sequence need not comprise a screening step. Sequences may also be identified from the knowledge of the skilled practitioner by sequence comparison methods using SEQ ID NO:1, for example, in mung bean, or where genome sequencing data is available or by reference to experience whenever the method is repeated on a host of a given type.

The question with respect to claims 57, 58, 61, 63 and 108-119 is not whether the material identified by carrying out a step in the method is described *a priori*, but whether the individual method steps of claims 57, 58 and 61 are described. The Office has not questioned the written description of any other aspect of the recited methods. The steps of the presently claimed methods are fully described so that a person of ordinary skill would recognize that the claimed method can be practiced on any of the recited hosts, and the inventors were in possession of the method as claimed at the time the application was filed.

Therefore, each of claims 57, 58, 61, 63 and 108-119 satisfy the written description requirement.

***Concerning claims 120-135***

Claims 120-123 recite sequences that are at least 50% homologous to SEQ ID NO:1 in language that was previously stricken from claims 49-52. Claims 124-135 depend from 57, 58, 61 and 12-122 and recite homologies of 70% to 80% and 95%.

Claims 124-129, which depend from and incorporate the method of claims 57, 58 and 61 and are adequately described for the reasons set forth above.

With respect to claims 120-123 and 130-135, the recited genus of sequences which are at least 50%, 70%-80% or 95% homologous with the sequence according to SEQ ID NO:1 comprise mathematically defined sets of sequences that could be instantly recognized by computer sequence comparison. Among these set of sequences, one skilled in the art would be able to predict sequences that would code for a protein having fucosyl transferase activity by reference to SEQ ID NO 1 as a representative species. For example, sequences having silent mutations, having mutations encoding conservative amino acid substitutions, and mutations that do not substantially disturb the conserved core sequence shown by SEQ ID NO: 3, which is described beginning at page 6 of the specification would be expected to have fucosyl transferase activity.

The Office has alleged that the specification does not provide sufficient guidance with respect to a conserved core structural motif. However, at page 6, the specification teaches that the conserved sequence of SEQ ID NO:3 is particularly useful for sequence recognition. (See also, Leiter et al. (1999), attached as Exhibit C, which functionally illustrates the cDNA sequence of the core fucosyltransferase.)

Furthermore, the recited degree of homology is consistent with the levels of homology seen among functionally identical fucosyl transferase enzymes. For example sequences encoding fucosyl transferase enzymes from mosses have nucleic acid identities of about 50-60% and are functionally the same at the enzyme level.

Therefore, SEQ ID NO:1 is in fact a representative of the recited genus and a person of ordinary skill in the art would recognize that the inventors were in fact in possession of the claimed invention at the time the application was filed.

For at least the foregoing reasons, withdrawal of the rejection is proper and is respectfully requested.

**Rejection under 35 U.S.C. § 112, enablement**

Claims 57, 58, 61, 63 and 108-119 have been rejected under 35 U.S.C. § 112, first paragraph, as allegedly not being supported by a disclosure that is enabling for the full scope of these claims. The Office has alleged that one in the art would have to perform an undue amount of trial and error experimentation in order to practice the invention as claimed. The rejection is respectfully traversed.

Claim 57 recites a step of identifying a DNA sequence in a host that codes for a protein having fucosyl transferase activity, the sequence comprising a selected DNA sequence having further defined characteristics. A biologically functional vector comprising at least 20 bases of the identified DNA sequence inversely oriented with respect to a promoter is then inserted into the host. Similarly, claims 58 and 61 recite a step of identifying a sequence encoding a protein having fucosyl transferase activity and additional defined characteristics and then using the identified sequence or portion(s) thereof. The selected sequences are further defined by being selected from among (A) a sequence according to SEQ ID NO: 1 with an open reading frame from base pair 211 to base pair 1740, (B) a sequence which is at least 50% homologous with the sequence according to SEQ ID NO 1, and (C) a sequence which hybridizes with the sequence according to SEQ ID NO: 1 under stringent conditions, wherein said stringent conditions comprise hybridizing in a solution comprising 7% sodium dodecyl sulfate, 0.5M NaPO4, and 1 mM EDTA at pH 7.0 and 50°C and washing with a 1% sodium dodecyl sulfate solution at 42°C. The Office has alleged that this step would require an undue amount of trial and error.

The Specification describes how to identify the sequences and provides an example of the step of identifying a DNA sequence in a host that codes for a protein having fucosyl

transferase activity, and in the process identifies a representative sequence. The identification step is fully described and can be performed on any of the recited hosts. At pages 18-19, the specification describes how to identify fucosyl transferase coding sequences in hosts using sequences from SEQ ID NO:1. At page 6, the specification teaches that the conserved sequence of SEQ ID NO:3 is particularly useful for sequence recognition.

As further evidence, Applicants provide the declaration of Prof. Dr. Iain Wilson (Attached as Exhibit D), which was prepared and submitted in the course of prosecuting the corresponding European application, which has been granted as EP 1 151 109 B1. (Note that the page references used in the declaration have changed for the present English translation of the application. For example the definition of the fucosyltransferase activity referred to in item 10 of the declaration can now be found on page 4, 4th and 5th paragraph and page 5 , 6th paragraph.).

To summarize Prof. Wilson's testimony, the definition and the assay to screen for the activity are sufficiently simple and are not ambiguous so that there is no an undue experimental burden for the skilled man in the art when identifying an enzyme having fucosyl transferase activity. Furthermore the scope of 50% homology is fully justified, because the genus of fucoslytransferases has homologies in the recited range. SEQ ID NO: 1, which was isolated from mung bean, has a 57% amino acid sequence identity to a fucosyltransferase isolated form *P. patens* (a moss).

Furthermore, examples of additional results achieved using the claimed methods are provided as Exhibit E, which show that the identification steps of claims 57, 58 and 61 are fully enabled by the teachings of the specification providing the representative sequence of SEQ ID NO:1 and the core sequence of SEQ ID NO:3, which can be used together with other

teachings of the specification and the knowledge of one of ordinary skill in the art to make and use the invention as claimed.

For at least the foregoing reasons, withdrawal of the rejection is proper and is respectfully requested.

**Rejection under 35 U.S.C. § 112, new matter**

Claims 49, 50, 57, 58 and 108-121 have been rejected under 35 U.S.C. § 112 as allegedly containing new matter. The rejection is traversed.

With respect to claim 58, the Office has alleged that the recitation of "at least 20 base pairs" is new matter. Similar allegations have been raised with respect to claims 50, 57 and 121, which recite variations of this language. Applicants submit that the recitation finds support at least at page 7 of the specification and in original claim 8, which recited a biologically functional vector, characterized in that it comprises a DNA molecule according to any one of claims 1 to 7, or parts thereof of different length, having at least 20 base pairs.

With respect to claims 49 and 120, the Office has alleged that the recitation of "at least about 50 consecutive nucleotides" is new matter. Applicants note that the first paragraph of page 9 includes support for the use of nucleotide sequences of more than 50 nucleotides. The specification also includes on page 8, the teaching that as much as all of the sequence of SEQ ID NO:1 may be inserted into a vector. Applicants further submit that the acknowledged descriptions of several ranges including more than 20 bases, 20 to 200 bases, 30-50 bases, 50 to 200 bases, in addition to the noted description of sequences greater than 50 nucleotides and sequences up to the whole sequence, provides ample implicit support for at least about 50 consecutive nucleotides in claims 49 and 120.

However, in order to reduce the number of issues in the present case, claims 49 and 120 have been amended to recite at least 20 consecutive nucleic acids, which clearly finds support in the specification at least at page 7 and in original claim 8.

Withdrawal of the rejections is respectfully requested.

## CONCLUSION

In view of the foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order. Such action is earnestly solicited.

In the event that there are any questions relating to this application, it would be appreciated if the Examiner would telephone the undersigned concerning such questions so that prosecution of this application may be expedited.

The Director is hereby authorized to charge any appropriate fees that may be required by this paper, and to credit any overpayment, to Deposit Account No. 02-4800.

Respectfully submitted,

BUCHANAN INGERSOLL & ROONEY PC

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